Social, Economic and Environmental Drivers of Zoonoses in Tanzania (SEEDZ)

Summary. This project will examine and assess the drivers, risks and impacts of zoonotic diseases affecting cattle, sheep and goats, and impacting on people's health, livelihoods and poverty, in northern Tanzania. As an interdisciplinary research project, it has considerable strategic relevance to the ZELS initiative: (i) focusing on **Tanzania** as a high priority area in terms of endemic zoonotic disease threats, with key lessons for other countries and regions; (ii) addressing three priority zoonoses - **brucellosis, Q fever and Rift Valley Fever** (RVF) – that have important impacts on human and animal health; and (iii) focusing on **livestock systems that are undergoing differential patterns of change**. The communities selected for the study represent diverse livestock systems (in peri-urban and pastoral contexts) that differ in their degree of connectivity to a rapidly growing urban centre, and that are therefore likely to differ in their response to social, economic and environmental drivers of change.

The research framework incorporates a livestock-human transmission model for endemic zoonoses embedded within contact network structures that respond to drivers of change. The research examines how these drivers influence human behaviour and livestock contact networks, and how these, in turn, affect transmission of zoonotic pathogens from livestock to people (Fig. 1).

The scientific significance of SEEDZ lies first in the scope of our goals for understanding how zoonoses affect, and are affected by, complex social and physical environments, and second in the diversity of scientific and policy perspectives. What makes this study unusual is that quantitative and qualitative data pertaining to all these elements will be collected coherently in one geographical system, explicitly integrating network patterns and infection dynamics with human economic incentives and behavioural response to predict emergent changes in disease risks. An important area of research lies in understanding the fundamental properties of network structures as they relate to the transmission of diseases, how human behaviour changes disease dynamics,[1] and how, in turn, changes or differences in disease dynamics induce changes in human behaviour.[2,3] The study is also significant in that the research design captures the dynamics of transition in terms of drivers of zoonotic disease risk, and provides an in-depth case study for assessing the impact of urbanisation on zoonotic diseases, which will have relevance for many areas undergoing rapid urban growth. A further novelty of our approach is highlighted by a DFID review which concluded that very few models of zoonotic diseases have sought to understand the perspectives and behaviours of farmers, consumers or policy-makers.[4,5]

This project therefore aims to use inter-disciplinary methodologies from qualitative social sciences, epidemiology and economics to identify and assess the important drivers of change in livestock systems in Tanzania and the implications for zoonotic threats affecting human health, livestock production and poverty in different communities.

These are ambitious objectives, but can be achieved by drawing on, and expanding, an experienced collaborative network for interdisciplinary research in Tanzania, and building on existing data and infrastructure. The project represents a major advance in our approach to understanding of zoonotic disease risks in the context of environmental, social, economic, demographic and governance changes that affect livestock production systems. The Tanzanian case is thus an exemplar for other areas where similar patterns of change are underway (e.g. many parts of sub-Saharan Africa), can be adapted for other zoonoses, and promises to advance methodology for integrative analyses in One Health research. The development impact of SEEDZ focuses primarily on institutional innovation, as well as shifts in policy processes, enabled by strong national and local stakeholder engagement from the outset.

Background. Complex social, economic, and environmental drivers, acting at local, regional and global levels, influence livestock ownership and management practices. East Africa is among the least urbanized areas of the world but is now experiencing rapid urbanisation.[6] Urbanisation is not only driving demand for meat and milk products among a growing affluent population,[7,8] but also leading to changing patterns of urban livestock-keeping.[9,10] In Tanzania: (i) the national livestock policy[11] promotes more sedentary lifestyles for pastoralists and the intensification of livestock production systems, which may increase disease risks for some zoonoses[12]; (ii) land-use pressures have resulted in conversion of rangelands to crop-based agriculture, with encroachment of livestock into wildlife areas, and vice versa;[13-15] and (iii) the dynamics of market

pricing combined with widespread access to mobile communications have major impacts on livestock trading and movement patterns[16]. However, the consequence of these changes on livestock-keeping practices and zoonotic disease risk are almost unknown[17]. SEEDZ has selected research sites that vary according to the pattern of change in livestock-keeping practices and degree of rural-urban connectivity in order to characterize important drivers of transition and understand their impacts on zoonotic disease risk.

For many infectious diseases, research has focused on identifying epidemiologically optimal solutions to disease problems. However, lack of understanding of behavioural, socio-economic and political dimensions can be a critical constraint to effective prevention and control, with health benefits remaining elusive. It is clearly not sufficient only to identify what needs to be done in scientific terms, but also to understand why people may or may not adopt recommendations that are shaped by formal epidemiological analysis. For example, it is known that some traditional food consumption practices can be risk factors for zoonoses, but recommendations to avoid risky behaviours need to address the economic or cultural imperatives that sustain these practices. Similarly, rational self-interest may lead to lower levels of vaccine uptake (both in people and livestock) than required for the epidemiologically or socially optimal scenario. The premise of this project is therefore that tangible benefits in terms of impact and engagement can be most effectively attained with a tighter weaving of quantitative and qualitative sciences.

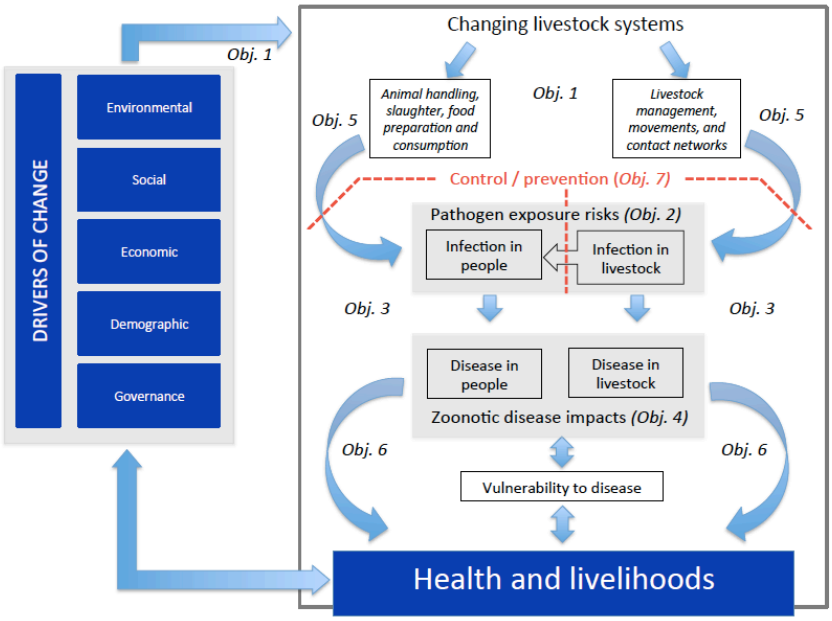

Fig. 1: Scheme describing the research framework and outlining the links between drivers of change, zoonotic disease risk and poverty impacts, mediated through changing contact networks and human behaviour.

Objectives. Through each of the following objectives, and synthesis across objectives, we aim to understand and quantify how risks for zoonotic disease (brucellosis, Q fever and RVF) in different livestock systems (peri-urban and pastoral) are affected by drivers of change. We aim to determine the impact of these diseases on health and livelihoods, and evaluate disease control strategies not only on the basis of their epidemiological rationale, but within the wider social and economic context. Specifically, we aim to:

1. Identify and evaluate the most important drivers of change in pastoral and peri-urban livestock systems in northern Tanzania and determine how these influence livestock ownership, management practices and contact networks.
2. Determine patterns of pathogen exposure through cross-sectional seroprevalence studies of zoonotic infections in linked human and livestock populations.
3. Determine the relative importance of different risk factors for transmission, acting at individual, household and community levels, and how these are influenced by drivers of change.
4. Determine relationships between zoonotic infection prevalence and disease, and the impact of these diseases on the health of human and livestock populations.

5. Incorporate data generated in Objs.1-4 into disease risk models that capture qualitative trends, human behaviour and decision-making.
6. Assess the impact of zoonotic diseases on family income and livelihoods to provide the evidence base for policy decisions relating to disease and poverty alleviation.
7. Examine and anticipate the likely acceptance and uptake of interventions for disease control and prevention based on models of disease risk.

Study sites. The region selected in northern Tanzania (Arusha Region) represents some of the most important livestock-owning areas in Tanzania in terms of high levels of livestock ownership, and differential rates of change in livestock ownership patterns. The sites comprise (a) peri-urban settings in Arusha city, (b) pastoral communities close (<100 km) to Arusha (Monduli District) and (c) pastoral communities further (>300km) from Arusha (e.g. Ngorongoro District). These pastoral sites are all experiencing changes in relation to patterns of mobility, wildlife and conservation policy, conversion of land to crop-based agriculture, and in-migration of other ethnic groups. We hypothesise that impacts of urbanisation are likely to be higher in communities living close to Arusha, than in more distant areas. Conversely, we anticipate that changes in wildlife and conservation policy are likely to affect livestock-keepers more in Ngorongoro than in Monduli.

Development and economic relevance. Tanzania is a **high-priority country for endemic zoonotic diseases**, with several interacting factors affecting disease risk, including high levels of poverty, a large proportion of the population engaged with livestock-keeping, a high prevalence of endemic zoonoses and an extensive wildlife-livestock interface.[18] The sub-Saharan livestock sector is a valuable resource that has enormous potential to support economic development.[19-21] Tanzania's livestock population is crucial to food security concerns of the region, and has the potential to support poverty alleviation through expansion of local and regional trade in livestock and livestock products, in line with national development policies.[20] However, these development benefits may need to be balanced against new zoonotic risks associated with emerging livestock systems. In addition to having direct impacts on human health, these zoonoses also affect livestock economies, food security and livelihoods through production losses, particularly reproduction and milk losses. Understanding zoonotic disease risks associated with urbanisation also has considerable development and economic relevance for Tanzania. In East Africa, most urban growth is occurring in and around mid-size cities with less than 500,000 inhabitants[6] as applies to Arusha municipality in northern Tanzania (pop. 416,442 in 2012). The implications for livestock systems are likely to be profound, with growing urban populations driving changing patterns of food consumption and livestock-keeping. However, rural-urban connectivity remains strong and dynamic,[6,22,23] and the increasing complexity of food supply chains that link pastoral and peri-urban communities to the centre has important implications for zoonotic disease risk.[17]

Understanding the burden of zoonoses will also require this project to address the problem of **mis-diagnosis of human febrile illness**, which partly arises from a lack of knowledge and awareness of zoonotic disease in Africa, a problem identified in all background DFID reports. Human febrile illness is one of the most common syndromes among hospitalized patients, but concerns are growing about high levels of misdiagnosis, particularly as malaria.[24] Recent studies by our group on **brucellosis** and **Q fever** indicate that these pathogens contribute substantially to human febrile illness in northern Tanzania, much more so than malaria.[25] Yet these diseases are almost unknown among medical practitioners and communities, and are still mostly diagnosed and treated as malaria, with major consequences for health.[26] **RVF** can also cause undifferentiated fever in humans and abortion/illness in livestock. However, a diagnosis of RVF is generally only considered during periods of high rainfall that are associated with major epidemics. There is growing evidence for circulation of RVF virus between epidemics (e.g. LaBeaud et al.[27]), which suggests that the burden and impact of RVF may have been overlooked. SEEDZ will support development of laboratory diagnostic capacity for RVF diagnosis and generate data that will contribute substantially to our knowledge of RVF epidemiology and impact in Tanzania.

This project has **high strategic relevance** to the ZELS initiative, targeting several priority areas identified in the consultation documents addressing: (a) a research focus in Tanzania, a country recognized as high priority in terms of endemic zoonotic disease threats;[18] (b) zoonoses, brucellosis, Q fever and RVF, which have been identified as priority diseases in DFID consultation documents[4,18,28] and reports of advisory groups of international agencies;[29] (c) diseases which are

likely to increase in impact under changing environmental conditions;[18] (d) important gaps in interdisciplinary research, in terms of integrating qualitative and quantitative expertise to provide an understanding of social, cultural, political, ecological and economic factors in disease prevention and control;[4,5] and (e) effective integration of policy-makers and capacity-building to strengthen national capability in complex system analysis and evaluation.[4]

Rationale for pathogen selection. Brucellosis, Q fever and **RVF** have been selected on the basis of their importance for human and animal health and strategic relevance, as described above. Several other factors were also important in pathogen selection: (a) the availability of reliable serological tests to generate seroprevalence data on human and livestock infections; (b) these pathogens represent different types of disease (e.g. different reservoir systems, different infectious periods) that will allow us to investigate how pathogens with different characteristics might be affected by changing local environments, contact network structures and human behaviours; (c) infection dynamics and impact are likely to be affected by the drivers of change that will be investigated in this study, including climatic factors (e.g. both high and low rainfall for RVF and Q fever respectively) and intensification of livestock systems (e.g. increased herd/flock size for brucellosis and Q fever); and (d) livestock vaccines are available for these pathogens, and although multiple routes of transmission exist, all can be transmitted through consumption of livestock products and contact with infected livestock, which provides a clear route to and link with policy interventions. Although we are requesting resources for generating serological data on these pathogens only, the framework will allow other zoonoses to be investigated using the samples and linked data collected by SEEDZ, for example, **anthrax, toxoplasmosis,** and **leptospirosis**. Furthermore, the research and modelling framework can be adapted to include other types of infection data (e.g. pathogen/strain prevalence) as capacity for implementing new diagnostic technologies advances.

Timeliness. SEEDZ is timely in focusing on livestock systems that are undergoing rapid rates of change and where the implications for zoonotic disease risks are still very uncertain.[18] With a decline in malaria in many parts of Africa, there is also growing concern about zoonotic causes of non-malaria febrile illness,[30,31] and this is reflected in our selection of zoonoses, all of which cause febrile illness. It is also timely in being able to build on substantial recent data and samples for linked livestock and human populations in northern Tanzania.

Relationship to previous and current research. Previous research conducted by our team provides substantial evidence that the selected zoonoses are widespread in East Africa, the disease impacts are severe, and disease risks likely to vary across different settings, e.g.: (a) brucellosis and Q fever are major causes of human febrile illness in Tanzania, causing 5 times as many cases of hospital admissions as malaria;[25] (b) *Brucella* seroprevalence patterns in livestock (4-12%) and people (7-10%) indicate widespread exposure, with hospital records indicating > 100 human cases/100,000/year in high-risk areas;[32, 33] (c) Q fever infection is widespread in humans and livestock across Africa, and the cause of acute respiratory illness in people in western Kenya;[34] and (d) recent laboratory results, arising from collaborative work of our team, demonstrate widespread inter-epidemic circulation of RVF virus in northern Tanzania.

Our collaborative network provides enormous added value, with on-going studies on endemic zoonoses (BB/J010367/1 - BACZOO) providing a core set of samples and data that will be used by SEEDZ, including data on brucellosis and Q fever seroprevalence, risk factors and disease impact in one of the sites (Monduli District) that will contribute to Objs. 2,3,4. SEEDZ includes new partnerships with qualitative social scientists and economists that will seek to understand and quantify the impact of zoonoses on poverty and livelihoods, and improve our understanding of decision-making and livestock practices at the household level, building on methodologies developed in current livestock disease research (BB/H009035/1 and BB/H009302/1) and introducing new ones, such as participatory network modelling. SEEDZ will interact with major interdisciplinary programmes exploring social, cultural, political and environmental drivers and effects of zoonotic disease emergence, such as the IDS STEPS-Centre led Dynamic Drivers of Disease in Africa Consortium (NERC/DFID/ESPA 2011 project) which includes a study of RVF in Kenya, and builds on work of the GU-Tanzania team investigating perceptions of febrile illness[26].

SEEDZ will also build on our development of models of disease transmission through livestock networks to investigate disease emergence and persistence, the role of network dynamics and

the relationship between epidemiological timescales and network structure (Wellcome Trust 070462/Z/03/Z and 081696/Z/06/Z[35-37]). Our group is also applying these models to the study of bovine tuberculosis transmission in Britain (DEFRA-SE3285) and to the relationship between network structure, disease persistence and farmer behaviour (Scottish Government A5251509).

Programme and Methodology. The research methodology reflects the objectives of the project to identify and assess important drivers of change in livestock systems in northern Tanzania and the impact of these changes on zoonotic disease threats affecting human, livestock production and poverty. These relationships will be compared across three sites - a peri-urban site (Arusha), and two pastoral sites (Monduli/Ngorongoro Districts) varying in relation to proximity to Arusha.

Rather than assign separate qualitative and quantitative approaches to achieve each of our objectives, we aim to weave methodologies for the generation and analysis of qualitative and quantitative data into the majority of the objectives (Objs.1,3,5,6,7). This requires interaction of all disciplines in the SEEDZ team, working together to shape and refine the research questions, in fieldwork and data collection, in modelling and analysis, and in engagement and impact activities.

Table 1. Proposed drivers of changes in livestock systems

Environmental	Wildlife and biodiversity, climate variability
Social	Gender relations/women's roles, education, food preparation and consumption
Economic	Cost of food, employment, mobile communication technology, transportation income levels, land tenure, land use, market structure and specialization
Demographic	Outmigration for employment, pastoral migration and settlement, urbanisation, household size and composition
Governance	International trade regulations, marketing regulations, land tenure, infrastructure, taxation, public health investments, veterinary services

Objective 1. To identify and evaluate the most important drivers of change in pastoral and peri-urban livestock systems in northern Tanzania and determine how these influence livestock ownership, management practices and contact networks.

We will undertake:

a) **A review** of census data, secondary literature on livestock, pastoral and peri-urban dynamics and policy documentation to: identify the proposed set of livestock system dimensions and drivers of changes; determine appropriate time-scales of change (most probably 20 years to represent a generation); and, identify and compile sources of data which may provide comparative data on the different drivers over an appropriate time scale. GIS and climate data will be compiled for the study areas and will include human and livestock census data, rainfall, data on wildlife distributions, and wildlife infection patterns (brucellosis/RVF). The project will also have access to remote-sensing data for part of the study area, obtained with the support of a GU PhD studentship (starting October 2013).

b) **Life histories** will be sampled purposively from livestock-owners attending local and regional markets. We will also explore life histories from people who are not livestock owners, but have access to and may interact frequently with livestock (including people with different tenure arrangements, women who are not considered owners, consumers etc.). Using the initial set of drivers as a framework, these life histories will have a livestock and disease focus to explore changes that people recall over the time scale (20 years), and what they perceive to be the key drivers of past and on-going changes. Targeted life histories will provide experiences of how these changes have affected different sections of the community by gender, age, ethnicity, education and relative wealth. For example, women's experiences of drought, livestock and disease might be very different to men's; community elders' reflections of how education or communication technology has affected livestock management may differ from perspectives of younger farmers.

c) **Key informant interviews** with policy makers, government officials, public health officials, vet and livestock officers, and wildlife managers, including those who can contribute to a longer-term perspective. Participants will be invited to policy-maker and livestock-keeper workshops for discussion of ideas and issues that capture both national and local

perspectives, and to initiate interactions between stakeholder groups for development of future policies that include the livestock sector, public health and wildlife managers.

d) **Transect walks** will be conducted with community members and livestock-keepers to explore understandings of landscape change in relation to perceived drivers.
e) **Characterisation of livestock contact networks** primarily in relation to movements and contacts to/from markets (assuming relative homogeneity of within-village and peri-urban contact structures). Livestock movements, including changing patterns of seasonal movement and market access, will be captured through key informant interviews for different categories of livestock work, including with the most influential livestock keepers. This will be complemented by interviews conducted at markets to understand origins and destinations of livestock coming through markets, and reasons for livestock owners and dealers to select particular markets for sale or purchase of livestock.
f) **Climate variability and land-use changes.** Perceptions of the nature of climate change and the implications of climate variability for land-use, household economics, and livestock management practices will be investigated through in-depth interviews within each site. Detailed local survey data will be linked with remote sensing data and other GIS data (e.g. digital elevation, soils, distance to wildlife protected areas) to allow generalization of local-survey data to landscape and regional scales, e.g. following the methods of Galvin et al.[38]

Triangulation methods will be used to assess the consistency and convergence of evidence obtained from different sources and methodologies, as well as to guide development of well-defined research questions in subsequent objectives. Indicative estimates for qualitative research – spread across the three research sites – are: Life histories: 60; interviews 120; key informant interviews 45; transect walks 6. In all instances, qualitative sample sizes will be determined through the concept of data saturation, rather than having a requisite pre-established number[39], while ensuring that we have sufficient data, both within each site and across research sites, to give us confidence in our conclusions.

Objective 2. To determine patterns of pathogen exposure through cross-sectional seroprevalence of zoonotic pathogen infections in linked livestock and human populations.

This will involve a **cross-sectional study** design consistent with that of the BACZOO project (BB/J010367/1), which is generating samples and data from pastoral communities in Monduli District. SEEDZ will extend cross-sectional sampling to new pastoral sites (Ngorongoro District), which are further from urban centres and more closely connected to wildlife protected areas, as well as peri-urban sites (Arusha) linked with pastoral systems, neither of which are included in the current project. The consistency in methodology across projects will allow us to exploit existing data and samples for model parameterization, while the extension through SEEDZ will allow us to capture variability in pastoral systems according to differential patterns of change, degree of connectivity to urban populations, and contact with wildlife that is not addressed in BACZOO.

The study design involves random sampling of households in each of 15 villages (or peri-urban equivalent), with up to 10 cattle and 10 sheep/goats sampled per household to yield ~ 1,500 samples (750 cattle, 750 sheep/goats) across the two new sites (adding to an existing 750 samples expected to be generated from Monduli through BACZOO in 2014). Conservatively assuming a seroprevalence of 50% (i.e. requiring the largest sample size), this should provide sufficient power to determine the prevalence of infection for each of the study pathogens with a desired absolute precision of 5% with 95% confidence intervals, assuming a design effect of 2.6, typical for a wide range of zoonoses in East Africa. Based on experience, it is anticipated that blood samples will be obtained from at least 4 people /household in each pastoral sites (~300 samples in each pastoral site, with lower numbers anticipated in peri-urban sites).

Serological assays will be carried out using methods established by BACZOO at KCMC with extension of laboratory diagnostic capacity to NMAIST.

Brucella spp. For both human and animal samples, a Rose Bengal Test (RBT) and competitive ELISA (AHVLA, UK) will be used to screen samples for antibodies to *Brucella* spp. using test protocols established and validated at KCMC.

Coxiella burnetii. An immunofluorescence assay (IFA), validated for testing human samples, will be used to screen human sera, and an ELISA (IDEXX Chekit Q fever test) to screen livestock

samples for IgG antibodies to phase II *C. burnetii* antigens, using protocols validated at KCMC in collaboration with reference laboratories (Washington Animal Disease Diagnostic Laboratory).

RVF. A recombinant nucleocapsid-based indirect ELISA for RVF IgG detection will be used to screen human and livestock sera (BDSL). In addition, the study will analyse sera using an IgG ELISA developed at MRC-University of Glasgow Centre for Virus Research using recombinant RVF nucleoprotein following the methods of Van Vuren et al.,[40] adopted for preliminary testing of wildlife and livestock sera from Tanzania, and which we aim to establish at KCMC and NMAIST.

Objective 3. To determine the relative importance of different risk factors for transmission, acting at individual, household and community levels, and how these are influenced by drivers of change.

A total of 30 focus group discussions will be held in pastoral and peri-urban communities to assess the significance of proposed drivers that have emerged from the purposive sampling (Obj.1). These sessions will draw on a prioritized and contextualized set of drivers and types of interaction with livestock (which are linked to potential transmission pathways), developed out of the life histories that have been gathered in Obj.1. Focus group studies will include participatory methods such as participatory mapping and matrix-ranking to understand the level and nature of disease recognition and the cultural logics of disease categories, aetiologies and perceptions of risk, and determinants of individual behaviour relating to principal transmission pathways (e.g. milk consumption, slaughter and carcass handling, milking, assisted parturition) in relation to gender and age, socio-economic status, education, ethnic group, religion, residence and migration history.

Qualitative data will be complemented by quantitative data on individual and household-level behaviour through cross-sectional questionnaires, linked with serological data. Risk factors for infection (seropositivity) will be quantified using hierarchical generalized linear models in R. For animal samples, explanatory variables will apply at three different scales: the individual (e.g. age, sex, origin), the herd/flock (e.g. herd/flock size, husbandry, movements) and the village (e.g. distance from cities, markets, conservation areas). For human samples, a similar hierarchy will exist, and infection in livestock (seropositivity) will also be included as a potential risk factor (presence or absence at the household level, ordinal prevalence at the village level). Power for the analysis of human risk factors was explored through simulation, and is estimated conservatively assuming a simple relationship between response (seropositivity) and explanatory variables (presence of infection in livestock). Results of these simulations, based on published seroprevalence rates for Q fever and brucellosis in East Africa, suggest that we have a greater than 80% chance of detecting odds ratios of between 1.9 and 2. 5 in pastoral areas. We anticipate that power will be lower in peri-urban areas, due to a smaller number of individuals sampled, and anticipate power enhancement through incorporation of additional domain data.

Objective 4. To determine relationships between zoonotic infection prevalence and disease, and the impact of these diseases on the health of human and livestock populations.

This objective will focus on events relating to livestock reproductive disease (abortion, stillbirths) reported through household surveys during cross-sectional surveys to allow linkage of livestock seroprevalence data and disease events. This activity would be further enhanced by surveillance networks and diagnostic capacity established by the abortion surveillance project (led by University of Nottingham), if funded. For human disease, the cross-sectional study will allow us to link livestock and human infection prevalence with occurrence of cases of human reproductive disease, fever and joint pain reported in household members during the previous year.

Data on the occurrence of **confirmed acute cases of brucellosis, Q fever and RVF** will be determined through on-going febrile surveillance studies established through the KCMC-Duke University collaboration, with serological diagnosis of cases based on from acute and convalescent samples of febrile patients admitted at KCMC and Mawenzi Regional Hospitals. Although these are tertiary referral hospitals that serve the study area, it is unlikely that confirmed cases will originate from the households randomly selected in our study. Our aim, therefore, is to use confirmed cases to determine patterns of human zoonotic disease and livestock infection only at the level of agro-ecological systems (i.e. pastoral or peri-urban).

Objective 5. To incorporate data generated in Objs.1-4 into disease risk models that capture qualitative trends, human behaviour and decision-making

Compartmental network models of disease formulated with a metapopulation structure will be developed to describe contact and transmission among and within households and communities, for peri-urban and rural agro-ecological systems. Dynamics for the target diseases will be analysed using parameters consistent with our knowledge of current conditions in our chosen systems. Determining which changes in the underlying contact structure and disease parameters produce the greatest model impact, assessed via both epidemiological and socio-economic metrics, will be used to guide the formulation of questions and collection of data on the behavioural drivers of contact and be used to inform Obj.6.

Activities under Obj.1 will identify important environmental and behavioural drivers of change in population contact structure. Two factors we expect to be important are changes in land tenure and livestock market structure, both of which can dramatically alter livestock contact and transmission patterns through changes in household livestock management and market activity. These activities can be viewed as being governed by strategic interactions representable by game-theoretic models. We will develop agent-based simulations augmented by analytical approaches developed from simple epidemiological models, social network analysis and economics (e.g. Althouse, 2010[41]). Strategic agent-based models, simulating decision-making in households, present an excellent opportunity for studying the interaction between livestock contact structure, livestock and disease management strategies and disease epidemiology over that landscape. While game-theory is well-established and widely applied in ecology, economics, sociology, and other fields, this research will contribute substantially to the empirics of epidemiological 'games' played on an explicit contact structure.

Analysis of qualitative data will generate understandings of trends that will guide the form of the mathematical relationships, and analyses of the resulting quantitative models will in turn inform the refinement of focus group discussion schedules. This iterative modelling framework will allow us to examine i) how changes in key factors, such as market structure and land tenure, could affect disease prevalence through changes in both the underlying epidemiological risks and behaviour responses, and ii) the epidemiological and economic consequences of proposed interventions for disease management while accounting for both direct epidemiological effects and indirect effect through economic behavioural response (see also Obj.7). Further, to the extent that private household incentives (e.g. private versus population-wide vaccination benefits) or constraints lead to deviations from desirable behavioural outcomes at the societal level, this framework will allow us to examine possible incentive instruments to bring private incentives and public health benefits into closer alignment.

Objective 6. To assess the impact of zoonotic diseases on family income and livelihoods

We will model household decision-making by adapting well-developed household production/consumption models[42,43] to the Tanzanian setting, focusing on the household decisions at the intersection of livestock health, human health, and other assets, including factors influencing transmission of diseases between livestock holdings, as developed in Obj.5. This household-level analysis will provide a basis for four related research outcomes, to: (a) inform the human behavioural components of the models; (b) understand the relationship between livestock heath (e.g. reproductive losses) and human health (e.g. febrile illness, chronic disability), and other household assets through household income effects; (c) provide a basis for estimating the household economic burden of zoonoses through the modelling framework; and (d) provide a basis for informing policy and intervention design through insights into how an intervention policy will induce change through household behavioural response.

Qualitatively, we will seek to understand whether and how households recognise brucellosis, Q fever and RVF as diseases that affect people and how transmission is understood. This in turn will lead to exploration of how families evaluate risk and cost (risk of disease for humans/animals and cost of disease for humans/animals). There is a strong recognition of the enormous cost of illness to poor families but little understanding of the trade-offs that households make between livestock production and human health. Such understandings will be drawn out through a small number (~20) of in-depth "social autopsies" with families who have been identified as having experienced both animal abortion/stillbirth and human fever simultaneously. The social autopsies,

for both human and animal illness, will seek to identify the cause of illness from the household perspective, the various "costs" of illness to the household, the strategies adopted to mitigate these costs and the understandings of good health that underlie these perspectives. These qualitative investigations will add nuance and complexity to the economic modelling work, to exemplify the personal experiences of how zoonotic disease affects people and their livelihoods.

This objective will also be supported by workshops to encourage communication between livestock-keepers and policy-makers. An innovative aspect of this will be to use social autopsies to provide accessible narratives to assist in breaking down barriers of confidence or education between different stakeholders.

Objective 7. To model the efficacy of interventions and examine their likely acceptance and uptake to provide the evidence base for policy decisions relating to disease control for poverty alleviation

This objective will bring together information generated through qualitative/participatory studies (Obj.1) and outputs of disease models (Obj.5) to identify potential interventions that will be both effective in reducing zoonotic disease risk and acceptable to livestock-keepers and families within different socio-economic contexts. We will consider interventions that include both prophylactic and reactive livestock vaccination strategies (with livestock vaccines potentially available for each of the study pathogens), and human behavioural changes (e.g. food consumption/preparation, livestock management practices). The modelling outputs from Obj.5 provide innovative ways of understanding the risks among those involved in the livestock value chain, while the qualitative assessment of the impact of zoonotic disease in different socio-economic contexts will promote the development of appropriate and practical interventions to minimise these risks.

Potential interventions for control and prevention of these zoonotic pathogens will be considered at household level (e.g. livestock vaccination/ management practices, food preparation/ consumption), community level (e.g. markets, trading practices) and national level (e.g. national brucellosis/RVF strategies). These interventions will be assessed using quantitative and qualitative methodologies to determine epidemiologically effective solutions within relevant socio-economic contexts. Rather than focusing on new technologies, this project aims to generate a much greater understanding of the social, economic and political constraints to implementing existing interventions, which will lead to **more effective uptake** and practical and immediate ways of minimising disease risks. The project will further catalyse **institutional change** by facilitating direct engagement between policy-makers and livestock-keepers through workshops, to provide greater mutual understanding of incentives and constraints operating at different levels.

Capacity-building will be integral to the project, and necessary for it to fulfil its objectives. Our capacity-building plan is targeted towards building a range of capacities, particularly focusing on the social sciences and modelling approaches, and attuned to the particular needs of African institutions but also emphasising mutual learning amongst all partners and wider stakeholders that will both enrich the project and extend beyond it. This engagement will include:

a) *Researchers from different disciplines*: building capacity for truly interdisciplinary conceptualisation and research, integrated field methodologies and analytical techniques. The project aims to build specific capacity for social sciences at NMAIST and SUA to support the development of interdisciplinary approaches in livestock and health research. We also aim to build on the strengths of NMAIST to support training of scientists with a background in physics, mathematics and engineering in integration of data with models for health research.
b) *Partners in government and university settings in Africa*: building capacity to understand research issues, engage in policy processes, and establish longer-term research-policy partnerships.
c) *Lab scientists and clinical practitioners*: establishment of RVF serological assays at KCMC, and for brucellosis, Q fever and RVF serology at NMAIST, providing support for validation of the RVF assay through the MRC-University of Glasgow Centre for Virus Research.
d) *Tanzanian graduate students* will be trained in interdisciplinary approaches involving joint mentoring programs and cross-cutting joint-authored publications. These students will be registered and funded through Tanzanian institutions (SUA, NMAIST), conducting their research with the project team in Tanzania. We will also apply for studentships through the DTP scheme and envisage pairing of Tanzanian and UK-based students.

e) Contributions to *capacity-building workshops* organized by other consortium partners (e.g. Afrique One, SACIDS, ICONZ), across east, west and southern Africa, which focus on interdisciplinary concepts and field methodologies.
f) *Development of teaching materials* (on zoonoses and One Health concepts, case study issues and themes) for courses at the STEPS Centre, Glasgow, NMAIST, NIMR and SUA, as well as partners in our capacity-building networks.

PROJECT TEAM. This project will involve **trans-national partnerships** between UK, Tanzanian and other international institutions. The precise roles of each of the team members is shown in the programme of work (below) and described further in the justification of resources.
University of Glasgow, UK (Cleaveland, Sharp, Matthews, Kao, Thomas, Shand) – overall coordination, science and research lead, field epidemiology, social sciences, modelling, GIS.
STEPS Centre, Institute of Development Studies (IDS), UK (Waldman, Leach, Marks) – social sciences, including anthropology, political science, capacity-building, communications and knowledge-exchange lead.
Nelson Mandela African Institute for Science and Technology, **Tanzania** (NMAIST) (Gwakisa) - lead institution in Tanzania, coordination of field research, and lead role in capacity building, including laboratory diagnostic capacity for brucellosis, Q fever and RVF serology
Kilimanjaro Christian Medical Centre-Duke University collaboration - (Ntabaye, Kibiki, Crump) – human health research and health policy liaison, laboratory diagnostic testing of archived sera at KCRI BL laboratory, human febrile illness surveillance.
Sokoine University of Agriculture (SUA) (Kazwala) – field epidemiology, capacity building.
Tanzania Wildlife Research Institute (TAWIRI) (Keyyu) – wildlife-livestock interactions, wildlife research and policy coordination, links with other ZELS projects in Tanzania.
Ministry of Livestock and Fisheries Development (Swai) **–** livestock systems, policy.
National Institute for Medical Research (NIMR) (Mfinanga) – human health research and ethical clearance applications, links with other ZELS projects in Tanzania.
Otago University (NZ) (Crump) – human infectious disease and diagnostic expertise, existing collaboration with Glasgow on bacterial zoonoses research.
Washington State University (Yoder, Lankester) – economic analyses, support for field studies.
FAO (Kivaria) – policy integration.

PROGRAMME OF WORK, OUTPUTS AND OUTCOMES, AND MILESTONES (proposed start date of 1st October 2014) - please also see Diagrammatic Work Plan

Objective 1. ***Outputs***: Knowledge and understanding of changes in livestock ownership and management practices, land-use, market access, wildlife and livestock policy, and environmental factors (e.g. rainfall, rangeland conversion); engagement between livestock-keepers and policy makers. ***Outcomes***: Policy decisions that anticipate future disease threats, enhanced uptake of appropriate interventions for disease control and prevention. ***Milestones***: Protocols developed and approved (Dec 2014); data compiled and policy reviews completed; GIS data compiled (Oct 2015); key informant interviews, participatory studies conducted; livestock market networks broadly characterised (Oct 2016); policy-farmer workshop conducted **(**Oct 2016)**.** ***Team:*** Involvement and interactions of all partners. The STEPS team (Waldman, Leach, communications officer, PDRA) together with policy partners (Kivaria, Swai, Keyyu, de Balogh) will focus on policy drivers at international, national and local levels; the GU social science team will focus on focus group studies, key informant interviews and participatory research at markets, supported by partners in Tanzania (Gwakisa, Kazwala, Keyyu, Lankester), and will engage with the modelling team (Matthews, Kao, Yoder). GIS data collection and analyses will be led by the UoG team (Thomas, Shand). This objective is likely to involve two SUA/NMAIST social science graduate students.

Objective 2. Outputs: Data on brucellosis, Q fever and RVF seroprevalence in people and livestock in traditional pastoral and peri-urban communities. ***Outcomes:*** Improved understanding of transmission links for model parameterisation and evaluation of interventions. ***Milestones:*** Protocols developed and approved (Mar 2015); serological assays established at KCMC and NMAIST (Oct 2015); human and livestock seroprevalence data generated in pastoral and urban

livestock communities of Arusha region, (Oct 2016). ***Team*****:** Cleaveland, Crump, Ntabaye, Kibiki, Gwakisa Kazwala, epi PDRA (GU), SUA/NMAIST MSc student.

Objective 3. ***Outputs:*** Qualitative understanding of factors affecting potential transmission pathways; quantitative data on risk factors for human and livestock infection. ***Outcomes***: Design of disease control strategies appropriate to different socio-economic contexts. ***Milestones*****:** Qualitative data generated through activities described in Obj.1 (Oct 2016), and within cross-sectional study villages (Oct 2016). Household surveys conducted (Oct 2016), data entered and risk factor analyses completed (mid 2017). ***Team:*** Sharp, Cleaveland, Crump, Kazala, Gwakisa, Lankester Matthews, Kao, social science and epidemiology PDRAs.

Objective 4*. Outputs:* Quantitative data on (a) relationship between infection prevalence and occurrence of disease syndromes in livestock and people, and (b) occurrence of cases of human febrile illness caused by brucellosis, Q fever and RVF in different livestock systems. ***Outcomes:*** Enhanced awareness of zoonoses among national and international policy-makers, and improved management of human febrile illness in Tanzania through enhanced clinical awareness. ***Milestones*****:** (a) cross-sectional study and analysis completed (mid 2017); (b) analysis of data generated through the KCMC-Duke febrile surveillance study (mid 2015). ***Team:*** Cleaveland, Gwakisa, Kazwala, Crump, Ntabaye, Mfinanga, epidemiology PDRA

Objective 5. ***Outputs.*** Compartmental network models and agent-based simulations that incorporate qualitative and quantitative data; understanding of factors affecting zoonotic disease risk, including human behaviour and economic incentives, and effectiveness of interventions. ***Outcomes.*** Design of interventions to tackle current and anticipated disease risks, incorporating economic and behavioural dimensions. ***Milestones*****:** Simple models parameterised using existing data (mid 2015); models fully developed (mid 2016); simulation outputs, including interventions (mid 2017). ***Team:*** Kao, Matthews, Yoder, modelling PDRA, supported by Cleaveland, Sharp, Waldman, Gwakisa, Kazwala, epidemiology and social science PDRAs.

Objective 6***: Outputs.*** Household-level economic models for pastoral and urban communities; quantitative and qualitative data on zoonotic disease impact on family income and livelihoods; social autopsies. ***Outcomes***. Development of evidence-based national and international health policy and prioritisation of zoonotic diseases. ***Milestones.*** Data collection instruments developed, field-tested (Mar 2015); economic model developed (end 2015) and parameterized (mid 2016); model outputs available (end 2016); social autopsies (mid 2016); production of public communication/workshop materials (end 2016). ***Team:*** Yoder, Lankester, WSU research assistant, supported by Cleaveland, Gwakisa, Kazwala, Sharp, Waldman, GU PDRAs.

Objective 7: *Outputs:* Data on effectiveness of intervention strategies; understanding of the likely acceptance of interventions at different levels; policy uptake of recommendations. ***Outcomes***: Mitigation of zoonotic disease burden through design of appropriate interventions and enhanced uptake. ***Milestones:*** Identification and preliminary assessment of potential intervention strategies for the three pathogens (mid 2015); qualitative data on issues affecting acceptance of these interventions at different levels (end 2015); development of simulation models that include intervention scenarios (mid 2016), outputs from simulations generated including intervention scenarios (mid 2017), communication and dissemination (early 2018) policy workshops (early 2018) ***Team***: All members will be involved in this objective.

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